IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Att. Docket: FISHMAN-4

In re patent application of:
Pnina FISHMAN
Appln. Serial No. 09/700,751
Filed: January 4, 2001
For: PHARMACEUTICAL COMPOSITIONS COMPRISING AN ADENOSINE RECPTOR ...

Group Art Unit: 1623
Examiner: J. Young
Washington, D.C.

DECLARATION
under Rule 132

Honorable Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir,

I, Pnina Fishman, an Israeli citizen residing at 19 Asher Barash Street, Herzlia, Israel, hereby declare:

1. I am the same Dr. Pnina Fishman, who submitted a Declaration under cover of an Amendment dated January 12, 2004. I have now noted that my previous Declaration was incorrectly dated January 11, 2003 and it should have been dated January 11, 2004.

2. I wanted to investigate the question whether the compound N^6-(Δ^2-isopentenyl)adenosine (IPA), disclosed in the Mittelman et al. reference (Annals New York Academy of Sciences, Vol. 255, pp. 225-234, 1975), cited by the Examiner in this case, can be regarded as an adenosine A3 receptor agonist. In order to answer this question, I purchased IPA from a commercial source (Sigma, USA) and sent this compound to a French service laboratory by the

name of Cerep and requested them to conduct binding studies of this compound to investigate the binding affinities thereof to the four known adenosine receptors: A_1, A_{2A}, A_{2B}, A_3.

3. A copy of the Cerep Report (Study Number 8842) of September 14, 2004 is attached. In the Report, IPA is referred to by an alternative trivial name 6-(γ,γ-dimethylallylamino)purine riboside. For the purpose of consistency, I will nonetheless refer to this compound as IPA. The Report is addressed to Dr. Sara Bar-Yehuda, who is a scientist in Can-Fite Biopharma and works under me and she took care of the formalities associated with this study, at all times under my direct supervision.

4. Once the Report was received in Can-Fite, I forwarded it to Dr. Adrian IJzerman for his review and my conclusion, similar to his, as expressed in a separate Declaration by him, is that IPA is not a selective A3 receptor agonist. Thus, when IPA is administered at a dose which will activate the A3 adenosine receptor it will invariably also bind and activate the A_1 receptor.

5. In comparison, please note, for example, that IB-MECA, which is an A3 adenosine receptor agonist, has a high selectivity to this receptor with IC_{50} and K_i which are about thousand folds higher than any other adenosine receptor (see clause 8 of my Declaration of January 11, 2004).

6. The undersigned declares further that all statements made herein of her own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with

the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: NOV. 17, 2004

P. Fishman

Prof. Pnina Fishman